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Prediction of Risk of Anterior Myocardial Infarction by Lesion Severity and Measurement Method of Stenoses in the Left Anterior Descending Coronary Distribution: A CASS Registry Study

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To assess the 3 year risk of anterior myocardial infarction in patients with left anterior descending coronary artery territory disease (30 to 100% stenosis), National Heart, Lung, and Blood Institute (NHLBI) Coronary Artery Surgery Study (CASS) registry patients were identified who were 1) medically treated, and 2) had evidence of viable anterior myocardium at the time of baseline angiography. Prospectively, 118 patients having an anterior infarction within 3 years of baseline angiography were identified from annual follow-up of 4,535 medically treated patients who had left anterior descending coronary artery disease and viable anterior myocardium. From the large residual pool of patients without infarction, 141 were randomly selected from a stratified matrix to represent the entire group. The maximal percent stenosis was estimated by the CASS multiple angiographers, by a current single observer rereading and by contemporary computer measurement techniques. Absolute lumen dimension was assessed by computer measurement.

The 3 year risk of anterior infarction was 2% for patients with their most severe left anterior descending stenosis <50%, 6% for patients with one such stenosis ≥50% and 11% for patients with two or more such stenoses ≥50% ($p < 0.02$). Stenoses of 90 to 98% had the highest (15%) 3 year risk of anterior myocardial infarction. The three methods used to measure maximal percent stenosis differed little with regard to their predictiveness. Absolute lumen dimension was less predictive of risk. These results may provide a more rational basis on which to base coronary revascularization decisions.

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Coronary artery disease is a diffuse and progressive disorder characterized by repetitive bouts of ischemia resulting from focal restriction to blood flow and by the more cataclysmic events of myocardial infarction and sudden death, more often the result of thrombosis (1) and arrhythmia (2,3). The angiographic determinants of survival in coronary artery disease (4–7) are fairly well understood. However, the relation between the degree of coronary narrowing and subsequent myocardial infarction in the absence of revascularization procedures is less well understood.

Prior retrospective studies (8–10) have established that new coronary occlusion, with or without associated clinical infarction, is related to initial severity of coronary stenosis. However, most of these retrospective studies were biased toward angiographic follow-up of patients with progression of symptoms. Moreover, these studies used subjective visual assessment of coronary stenosis, which has a variability ranging from 5 to 18% in reported series (11,12). To more accurately and reproducibly assess coronary stenosis severity, computer algorithms have been developed for luminal edge detection and stenosis quantitation. Dimensional accuracies of ±150 μm have been claimed (13); however, these or similar methods have been applied only in limited numbers of patients to the study of risk of occlusion (14) or the progression of coronary artery disease (15,16).

The National Heart, Lung, and Blood Institute (NHLBI)

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sponsored Coronary Artery Surgery Study (CASS) data base of medically treated patients, which contains descriptions of entry coronary angiograms and subsequent mandatory clinical follow-up, provided the opportunity for a large prospective study. Using occurrence of myocardial infarction as an end point, we could study the risk of subsequent infarction in relation to the initial severity of coronary stenosis. Moreover, the extent to which subjective visual assessment versus computer assisted quantitation affected assessment of lesion severity and, thus, subsequent risk of myocardial infarction, could be considered.

Methods

CASS is a NHLBI-sponsored multiinstitutional research project consisting of a randomized trial of the medical versus surgical treatment of coronary artery disease and a substantially larger registry of patients who underwent diagnostic evaluation including coronary angiography for suspected coronary artery disease. These patients were carefully followed up for subsequent cardiac events. Extensive historical, physical examination and laboratory data were obtained for each patient at the time of entry into CASS. The details of data entry have been reported elsewhere (17).

Patient selection. Between August 1974 and May 1979, 18,894 men and 6,065 women underwent coronary arteriography for proved or suspected coronary artery disease at one of the 15 CASS clinical centers. Anterior myocardial infarction was chosen as the end point for this study because it more closely correlates with stenosis in one vessel than does inferior or lateral infarction; that is, the cause and effect relation is more easily presumed. Criteria for entry into this study of the angiographic antecedents of anterior myocardial infarction were:

1. No evidence of prior anterior myocardial infarction: a) The baseline electrocardiogram (ECG) had no pathologic Q waves in leads V_1 to V_4. b) Absence of severe hypokinesia, akinesia or dyskinesia in the anterobasal, anterolateral and apical segments on the baseline right anterior oblique left ventricular angiogram. In essence, retained wall motion in the myocardial distribution of the left anterior descending coronary artery was required.

2. Demonstration of left anterior descending coronary artery disease in the absence of left main coronary artery disease on the baseline arteriogram: patients with an entirely normal or minimally abnormal left anterior descending coronary system were not included because prior studies have already demonstrated a relatively benign prognosis for patients with this angiographic pattern. a) 30 to 100% diameter stenosis in one or more segments of the left anterior descending coronary artery (proximal, mid, distal or major diagonal branch) on the baseline angiogram. b) Left main coronary artery stenosis <30% on the baseline angiogram.

3. Medical treatment and annual follow-up of 3 years' duration: patients were considered as medically treated until 3 years had elapsed. Patients having coronary surgery were considered medically treated up until the date of surgery, at which time they were "censored" from the study.

4. Angiographic quality sufficient to allow quantitative assessment of the severity of the anterior descending coronary stenosis.

A total of 4,535 patients met these preliminary criteria (Fig. 1).

Patient follow-up. Clinical follow-up, performed at regional centers at yearly intervals (17), included specific querying of patients regarding hospitalizations or possible acute coronary events. Electrocardiographic and cardiac enzyme data were obtained for all suspected cases of myocardial infarction including all hospitalizations of >5 days' duration and all deaths. Necropsy data were reviewed, when available, for all suspected cardiac deaths. Data were prospectively recorded on standarized forms (17). All cases of anterior myocardial infarction were identified that had a date of occurrence within 3 years of angiography and were not preceded by coronary surgery.

Anterior infarction group. For the purposes of this study, anterior myocardial infarction was based on a clinical diagnosis validated by a combination of ECG changes or enzyme elevations, or both, which were either diagnostic or strongly suggestive of myocardial infarction. This diagnosis was established by individual clinical site review of hospitalization records on all admissions of CASS patients for suspected myocardial infarction. Infarction diagnosis required a combination of one or more of the following: new Q waves on ECG, evolutionary ST-T wave segment changes and serum enzyme changes; typically, the patient was hospitalized >5 days. Silent anterior infarction was identified by the presence of new significant Q waves in leads V_1 to V_4 on any follow-up ECG within 3 years of angiography. To establish that an infarction was most likely due to an occlusion within the left anterior descending artery distribution, it was required that the major ECG changes (new significant anterior Q waves, ST segment depression or elevation or T wave changes) be located in leads V_1 to V_4.

A total of 224 patients were identified from the CASS data base as meeting the criteria for anterior infarction within 3 years of angiography without intervening coronary surgery. Their baseline cineangiograms were requested from the participating CASS centers; angiograms from 132 patients were obtained within a 6 month deadline. The 92 angiograms not obtained either had been routinely discarded or were not otherwise readily locatable; however, there did not appear to be any cine retrieval bias that would affect the study results. Six cineangiograms were eliminated because of poor quality and eight were eliminated because on review they failed to meet entry criteria (for example, obvious anterior wall akinesia or no anterior descending territory stenoses discernible by two observers). One hundred eighteen patients

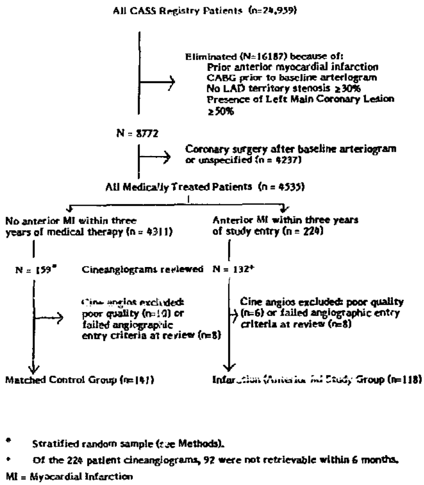

Figure 1. Flow diagram defining the study inclusion and exclusion criteria and number of patients in each category.

with anterior myocardial infarction were entered into the study (Fig. 1). Of these, 61 had transmural anterior myocardial infarction, 52 had nontransmural anterior infarction and 5 had silent anterior infarction.

Matched control group. Of the 4,535 patients who met the initial entry criteria for the study, 4,311 did not have an anterior myocardial infarction within the 3 year follow-up period. Three patients without infarction were randomly identified from within 48 angiographically defined strata for each patient with infarction. The details of this stratification are specified in the Statistical Methods section. The first matched cineangiogram arriving for review was used in the analysis. Because angiograms were read in batches, occasionally two control patients were obtained for each patient with infarction. Eighteen cineangiograms reviewed as potential "controls" were excluded because of poor quality (10 patients) or because of failure to meet criteria on review (8 patients). Precise angiographic 1:1 equivalency of the control group to the anterior infarction group was affected by these exclusions and by random availability of cineangiographic films. To adjust for multiplicity of control patients without eliminating acquired data, and to adjust for the number of patients analyzed for each strata relative to the proportion of patients in each strata from the entire medically treated population, a statistical "offset" term was required (see Table 1).

Visual assessment of the severity of coronary stenosis. The original CASS readings for all angiograms performed from 1974 through 1979 were obtained from the CASS Coordinating Center data base. The left anterior descending coronary artery and its major branches were segmented into proximal, mid and distal anterior descending artery and major diagonal branches. The percent stenosis for all lesions in the anterior descending distribution was assessed by the angiographers at each of the CASS clinical sites, as influenced by periodic review meetings and monitoring by the CASS central angiographic review panel. These are referred to as multisite, multiobserver observations and were permanently recorded shortly after each baseline arteriogram.

An additional visual assessment of percent stenosis was provided by a single observer (S.E.), who reread all of the angiograms of patients judged to have left anterior descending territory stenoses, was unaware of the patients' clinical outcome (anterior myocardial infarction or control) and did not know the prior angiographic interpretations. The purpose of the additional single observer was to determine the extent of correlation with the previous multiobserver estimates of percent diameter reduction. Although neither ruler nor caliper was used to measure percent stenosis, a rigorous and consistent approach toward estimating was followed. All single observer estimates were made before the computer-assisted quantitation.

Table 1. Angiographic Characteristics of Patients Studied

	Nonanterior MI Groups		Anterior MI Groups		
	All Patients: Group A (n = 4311) (%)	Matched Control: Group B (n = 141) (%)	All Patients: Group C (n = 224) (%)	Anterior MI Group: Group D (n = 118) (%)	Offset*
Single vessel disease					
with LAD 30 to 49%	283 (7)	2 (1)	3 (1)	1 (1)	3.85
50 to 69%	306 (7)	5 (4)	5 (2)	4 (3)	3.89
70 to 99%	537 (12)	20 (14)	31 (14)	17 (14)	2.69
100%	199 (5)	9 (6)	9 (4)	6 (5)	2.69
Multivessel disease					
with LAD 30 to 49%	727 (17)	15 (11)	16 (7)	10 (8)	3.41
50 to 69%	716 (16)	14 (10)	31 (14)	11 (9)	2.90
70 to 99%	1207 (28)	54 (38)	96 (43)	49 (43)	2.43
100%	336 (8)	22 (16)	33 (15)	20 (17)	2.23
Total	4311 (100)	141 (100)	224 (100)	118 (100)	

*Offset = $\log_e\left(\frac{\text{Group D/Group C}}{\text{Group B/Group A}}\right)$. Offset is an adjustment for the proportional representation of particular angiographic subsets within the control group versus patients in the anterior MI group. LAD = left anterior descending artery; MI = myocardial infarction; n = number of patients.

Each stenosis in the left anterior descending artery or any of its major diagonal branches that was visually ≥30% reduction in luminal diameter was individually graded. Percent diameter reduction was defined as the diameter of the maximal contrast boundary of the stenotic area referenced against the maximal contrast boundary of a contiguous normal-appearing reference segment. Both the maximal percent diameter reduction in any projection and the mean percent diameter reduction in orthogonal views were estimated. For the high grade stenoses, when these were more difficult to judge, a score of 95% was used for lesions with very small but discernible lumens. Ninety-nine percent was used for barely discernible lumens with slowed anterograde flow and 100% for stenoses that had no anterograde flow, except for that provided by collateral vessels. In addition, the territorial distribution of each terminal coronary branch (diagonals, terminal anterior descending artery) was scored for size: small = 1, medium = 2 and large = 3. For the purposes of this analysis, only stenoses subserving territorial distributions scored ≥2 were considered.

Computer assisted quantitation of the severity of coronary stenosis. Angiograms were reviewed on a Vanguard M35C projector equipped with a movable stage and a three-lens turret, which provided optical magnification at ratios of 1:1, 3.7:1 or 7:1. Cine frames were selected to visualize the stenosis as nearly as possible perpendicular to the X-ray beam at end-diastole in two orthogonal views. A wide band video camera acquired the selected image in a 512 line format that was then digitized by a De Anza image processor 480 × 512 (8 bit gray scale). The operator used a light pen to trace approximations of the coronary catheter edges at a point proximal to the tip taper. Using these lines as initial search locations, the automatic edge-finding algorithm then drew and smoothed the catheter edge, defining the catheter edge at the peak of the first derivative of the gray scale density gradient, perpendicular to the long axis of the catheter (18). The computer then derived the catheter diameter from a 2 mm long region indicated by the operator. The outer dimension of the catheter used for selective contrast injection into the artery was manually entered into the computer and used as the reference dimension for each cine run. Catheter diameters were entered as follows: Judkins 7 F = 2.3 mm, Judkins 8F = 2.6 mm, Sones 7F = 2.4 mm (at the shaft) and 1.8 mm (at the tip), Sones 8F = 2.7 mm (at the shaft) and 1.8 mm (at the tip), Bourassa 7F = 2.5 mm, Bourassa 8F = 2.7 mm. If the catheter type was not known (19% of the cases) the diameter was entered as 2.5 mm.

In a similar manner the margins of each coronary stenosis and an adjacent "normal" coronary segment (usually that segment just proximal to the stenosis) were traced by the computer, which measured the precise segment diameters by using the catheter measurement on the same cine run for calibration (Fig. 2). The computer then determined the minimal residual lumen diameter in absolute dimensions and the percent stenosis relative to the "normal" coronary segment. The accuracy of this method in determining diameters of artery phantoms was previously determined to be ±3.9% (18). Mean percent stenosis was obtained by averaging the results in the orthogonal projections. If the stenosis was well visualized only in one projection, the value from that projection was also used as the mean.

Statistical Methods

Selection of control patients. All 4,535 medically treated patients were stratified into 48 "cells." This stratification

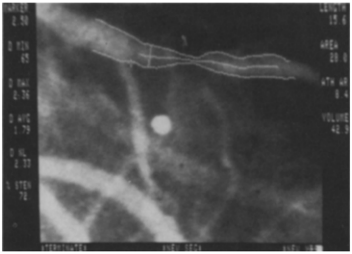

Figure 2. Computer determination of percent stenosis (% sten) and minimal residual lumen diameter (D min) for a proximal left anterior descending artery stenosis. Arterial boundaries are compute determined. "Normal" diameter has been entered by the operator. Calibration by measurement of the catheter tip is not shown.

was based on coronary dominance (right, left or balanced), the percent luminal diameter reduction (30 to 49, 50 to 69, 70 to 99 and 100%) of the most severe anterior descending coronary artery lesion by the original CASS multisite, multiobserver estimate and the maximal extent of concomitant right and circumflex coronary artery disease (0 to 29% and 30 to 100% for each vessel). Within each cell, each patient with infarction was matched for analysis with patients without infarction. In the present analysis, we analyze the prognostic value of one of the stratification factors, namely, percent stenosis in the anterior descending artery, which was measured in five different ways. A logistic regression technique was used to compute the probability of anterior infarction for particular angiographic patient subgroups based on an analysis of the most severe left anterior descending territory stenosis.

The five grading methods for maximal percent stenosis. 1. Original multicenter, multiobserver single plane CASS reading of maximal percent stenosis (previously recorded in the CASS study data base). 2. Single observer, single plane reading of maximal percent stenosis (maximum in any view). 3. Single observer, orthogonal plane reading of maximal percent stenosis (mean of two views). 4. Computer-assisted, single plane reading of maximal percent stenosis (maximum in any view). 5. Computer-assisted, orthogonal plane reading of maximal percent stenosis (mean of two views).

Statistics. The data were analyzed using logistic regression methods developed and validated previously for use in case control studies with nonrandom sampling (19). The patients included in this study consist of a sample of 118 cases taken from the population of cases (that is, medically treated patients with anterior infarction within 3 years) plus a sample of 141 control patients taken from the control population (that is, medically treated patients without infarction). If the study sample had been a simple random sample from the entire population, a standard logistic regression analysis could have been used. However, the study sample is biased because infarction cases are oversampled relative to control cases and some stratification cells are oversampled because of matching. Thus, a standard logistic regression would produce biased estimates of the risk of infarction, and an analysis method, which adjusts for the biased sampling, was required (19). This approach is possible because the numbers of infarction cases and control cases in the sample and the population are known for each of the 48 stratification cells. Thus, an "offset" term (19) could be utilized to adjust for the proportional representation in particular angiographic subsets of infarction and noninfarction patients. For the purpose of these calculations, the population of medically treated patients is defined as those patients who did not have bypass surgery within a site-specific time period after entry to CASS (20), usually about 4 months.

Results

Characteristics of the infarction and control patients. Table 2 shows pertinent clinical and angiographic features of the infarction and noninfarction populations as a whole and the study patients for each group. The study patients with anterior infarction are representative of the total infarction population in terms of age, gender, Canadian Heart Association angina class, and angiographic extent and severity of coronary disease. This equivalency suggests that no selection bias was incurred either by the random matching process used to select the control patients or as a result of unavailable or excluded cineangiograms in both the control and the anterior myocardial infarction groups.

Table 1 shows the categorization of patients into eight angiographic subgroups that provided a basis for determining the offset factors used in the statistical analysis. Although the angiographic distribution of both the anterior myocardial infarction and matched control study groups was generally similar to that of the respective populations from which they were drawn, the computed offset was required to adjust for residual bias in the control group resulting from matching of control patients with patients with infarction. This matching gives the control study group somewhat more severe coronary artery disease than that of the overall noninfarction population.

Computer versus visual assessment of the degree of stenosis. A total of 557 lesions in the left anterior descending distribution were measured by the original CASS angiographers, by a current single observer and by a computer using automatic edge detection. Table 3 compares the computer assessment of maximal percent stenosis (single plane read-

Table 2. Clinical Characteristics of Patients Studied

	Noninfarction Groups		Anterior Infarction Groups	
	All Patients (n = 4311)	Matched Control Group (n = 141)	All Patients (n = 225)	Anterior MI Group (n = 118)
Age (yr)	53.2 ± 8.8	53.8 ± 8.7	54.0 ± 9.6	53.2 ± 9.8
Gender (% male)	77.9	78.0	82.2	87.3
CHA angina class (%)*				
0 to I	33.1	27.7	24.4	27.1
2	30.5	29.8	31.6	36.4
3 to 4	27.9	32.6	36.5	29.7
Congestive heart failure class III to IV (%)	2.1	2.1	3.1	2.5
Number of vessels with ≥70% stenosis (%)				
0 to 1	55	42	34	37
2	27	29	33	31
3	18	29	32	32

*Percentages do not total 100% because some patients had angina unrelated to exertion; CHA = Canadian Heart Association; other abbreviations as in Table 1.

ing) with the single observer and multiple observer (CASS) visual assessment of maximal percent stenosis for each patient. In general, the CASS multiobserver assessment reported a higher percent stenosis than that of the computer-assisted algorithm in the experienced single observer estimate for stenoses in the range of 30 to 89%. The single observer determination correlated more closely with the computer result. The combined variability for both the multiobserver and single observer visual assessments averaged 14.1 ± 11.8% and was highest for stenoses of 30 to 49% and lowest for high grade stenoses. Variation between repeated computer measurements averaged 5.5 ± 7.2%, which was substantially below that of visual interpretation ($p < 0.05$).

Table 3. Methods for Grading Stenosis

A. Comparison of Methods for Grading Stenosis (%)*

Computer Single Plane (range [%])	Computer (mean ± SD)	Single Observer (mean ± SD)	CASS Multiobserver Multicenter (mean ± SD)
30 to 49	39 ± 7	37 ± 9	52 ± 20
50 to 60	59 ± 5	61 ± 16	68 ± 19
70 to 89	78 ± 5	84 ± 12	87 ± 16
90 to 100	99 ± 3	99 ± 2	95 ± 14

B. Correlations Between Different Methods for Grading Stenosis

CASS multiobserver vs single observer (maximal or orthogonal planes): 0.76 to 0.78.

Single observer (maximal or orthogonal) versus computer (max or orthogonal): 0.94 to 0.96.

CASS multiobserver vs computer (maximal or orthogonal planes): 0.75 to 0.76.

*All single plane reading of maximal stenosis; CASS = Coronary Artery Surgery Study; SD = standard deviation.

Prediction of anterior infarction. The risk of anterior myocardial infarction for the total population of 4,535 patients with left anterior descending disease over the subsequent 3 years was 4.9%. Table 4 shows the estimated risk of infarction for each of the six methods evaluated. Each method of evaluating percent stenosis achieved predictive value of infarction at $p < 0.001$. All methods were similar with regard to their predictiveness for subsequent infarction. Risk of anterior infarction by all methods was low for stenoses <50% (range 1.9 to 2.3%), maximal for 90 to 98% stenoses (range 7.1 to 30.9%) and somewhat lower for total or subtotal stenoses of 99 to 100% (range 7.1 to 8.0%). The absolute minimal residual lumen diameter data were less predictive of subsequent infarction ($p = 0.02$). The 95% confidence intervals in Table 4 shows considerable overlap of risk among the various angiographic categories. If only stenoses in the proximal or mid left anterior descending coronary artery were analyzed by these same methods, the predictive value of the methods was similar (for example, for computer maximal percent stenosis: all stenoses chi-square = 21.3, proximal and mid-stenosis chi-square = 20.9), but the risk of infarction within each subset was slightly higher if only proximal and mid-stenoses were evaluated (8.5 ± 5.5% versus 7.7 ± 5.8%, $p = 0.06$).

Because changes in medical therapy may have an impact on progression to myocardial infarction, and because the study patients were enrolled from 1974 through 1979 and follow-up data analyzed for an additional 3 years, we examined the results for potential effects of medication. A relatively small proportion (5.5%) of patients in this study were receiving antiplatelet drugs. Calcium channel blocking drugs were not yet available in the United States during the time span covered by this study. One hundred thirty-two (52%) of

Table 4. Estimated Probability of Anterior Myocardial Infarction Within 3 Years Comparing Seven Left Anterior Descending Coronary Artery Lesion Grading Methods

Arbitrary Categorization	n	Probability of Anterior MI (%)	95% Confidence Interval for the Probability of Anterior MI (%)	Chi-Square/p Value Based on Arbitrary Categorization (col. 1)	Chi-Square/p Value Based on Quintile Categorization*
CASS % stenosis					
0 to 49	58	2.0	1.2 to 3.6	17.8	18.4
50 to 69	42	5.5	3.0 to 9.9	$p = 0.001$	$p = 0.001$
70 to 89	68	8.2	5.2 to 12.6		
90 to 98	35	7.1	3.8 to 13.0		
99 to 100	56	7.3	4.4 to 11.8		
Single observer					
maximal % stenosis in any view					
0 to 49	65	1.9	1.1 to 3.2	22.5	18.1
50 to 69	50	6.5	3.8 to 11.0	$p \le 0.001$	$p = 0.001$
70 to 89	54	7.3	4.4 to 11.9		
90 to 98	29	9.1	4.6 to 17.3		
99 to 100	61	8.0	5.0 to 12.6		
mean % stenosis (orthogonal views)					
0 to 49	80	2.4	1.5 to 3.8	19.5	15.5
50 to 69	57	7.3	4.4 to 11.9	$p \le 0.001$	$p = 0.004$
70 to 89	46	6.6	3.8 to 11.3		
90 to 98	21	11.2	4.9 to 23.5		
99 to 100	56	7.9	4.8 to 12.7		
Computer					
maximal % stenosis in any view					
0 to 49	62	2.0	1.1 to 3.4	21.5	21.6
50 to 69	90	6.6	4.4 to 9.7	$p < 0.001$	$p < 0.001$
70 to 69	42	8.2	4.6 to 14.1		
90 to 98	10	15.3	4.4 to 41.3		
99 to 100	55	7.1	4.3 to 11.5		
mean of maximal % stenosis in orthogonal views					
0 to 49	73	2.3	1.4 to 3.9	21.3	18.9
50 to 69	94	6.3	4.3 to 9.3	$p \le 0.001$	$p = 0.001$
70 to 89	31	9.9	5.1 to 18.4		
90 to 98	6	30.9	4.9 to 79.4		
99 to 100	55	7.1	4.3 to 11.5		
Residual lumen diameter (mm) (minimum in any view)					
0.0 to 0.4	69	7.8	5.0 to 12.0	11.3	9.1
0.5 to 0.9	45	8.8	5.0 to 14.8	$p = 0.02$	$p = 0.02$
1.0 to 1.4	73	5.0	3.2 to 7.9		
1.5 to 1.9	37	2.9	1.4 to 5.6		
>2.0	34	3.3	1.7 to 6.4		
Residual lumen diameter (mm) (mean of orthogonal view)					
0.0 to 0.4	64	8.5	5.4 to 13.2	8.3	4.9
0.5 to 0.9	38	7.1	3.9 to 12.7	$p = 0.08$	$p = 0.30$
1.0 to 1.4	78	5.1	3.3 to 7.8		
1.5 to 1.9	38	4.0	2.1 to 7.6		
>2.0	40	3.2	1.7 to 5.9		

*The number of patients (n) determined by quintile distribution is set to be equal in each subgroup; whereas, arbitrary categorization yields unequal numbers in each group (column 2). Abbreviations as in Table 1.

Table 5. Three Year Risk of Anterior Infarction (%): Evaluation of Effect of Multiple Stenoses*

Number of Left Anterior Descending Territory Stenoses ≥50%	3 Year Risk of Anterior Infarction* (%)
0	1.9 (65)
1	5.9 (114)
≥2	10.7 (80)
All	5.5 (259)
$X^2 = 26.7$, $p < 0.0001$	

*Number of instances is given within parentheses.

the 259 patients in this study received beta-adrenergic blocking drugs. In general, these patients had more severe angina (38.8% had class III or IV angina versus 31.3% in the nonbeta blocker therapy group), but were otherwise similar to those patients not receiving beta-blocking agents. Those patients who received beta-blocking drugs had a lower 3 year risk of anterior infarction than did those not receiving beta-blocking drugs (4.4 versus 5.3%, $p < 0.05$). This relative reduction of risk in patients taking beta-blocking drugs was noted primarily in patients with stenoses <70% (relative risk reduction = 0.64 by the computer-assessed maximal method) and with 90 to 98% stenoses (relative risk reduction = 0.66).

The effect of multiple left anterior descending coronary artery territory stenoses of ≥50% narrowing on 3 year risk of anterior myocardial infarction is shown in Table 5. The number of stenoses ≥50% was the primary prognostic determinant (chi-square = 26.7 with two degrees of freedom; $p < 0.001$). The number of lesions <50% was not prognostic (chi-square = 3.9 with 6° of freedom; $p = 0.07$).

Discussion

Features of the study groups. The overall 3 year risk of anterior myocardial infarction in these medically treated patients was 4.9%. This figure, and all the results described herein, must be viewed with an understanding of the selection criteria. The study groups comprised patients in CASS receiving medical therapy for 3 years after initial angiography and comprised 48% of all patients with left anterior descending territory disease. The 52% nonmedically treated patients were surgically treated and generally had greater severity of both angina and coronary disease, potentially biasing the medically treated study groups toward more benign coronary disease. Thus, the estimates of anterior infarction rates and prediction of infarction risk may be underestimated in this study and provide a lower limit of angiographic risk.

Conversely, medical therapy from 1974 to 1982 did not include as extensive use of beta-adrenergic blocking drugs as is current practice. Infarction risk for patients taking a beta-blocking drug was 21% lower than for patients not taking a beta-blocking drug, a result that suggests that current patient management might yield lower myocardial infarction rates than those of the study patients. The current use of antiplatelet drugs (21) and calcium channel blocking drugs also may have a beneficial effect on risk of infarction (22,23), but cannot be evaluated in this study because too few patients were taking these drugs.

Nonetheless, the CASS registry provides a unique angiographic library with unbiased and structured clinical follow-up providing a basis for prospective assessment of clinical outcomes in patients with particular angiographic patterns. The number of patients from whom risk of infarction can be determined is larger in this study than for any other study attempting to relate objective measurements of stenosis severity to risk of infarction.

Prognostic role of severity of left anterior descending coronary stenosis. The results of this study demonstrated that there is an appreciable, but small, risk of infarction when the most severe left anterior descending coronary artery lesion is 30 to 49% severity, and that this risk increases substantially as stenoses equal or exceed 50% reduction in luminal dimension. Although the risk of anterior myocardial infarction did tend to increase in angiographic categories of >50% stenosis, these differences, when compared, were not always statistically significant (single observer maximal percent stenosis: chi-square = 1.41, p = NS; computer maximal percent stenosis: chi-square = 3.58, p = 0.04). Thus, the risk of anterior myocardial infarction for the 3 years after angiography is elevated once the 50% threshold is crossed. However, small gradations of percent stenosis >50% make little difference except that stenoses of 90 to 98% may pose a particularly high risk. This is at variance with the report of Harris et al. (24) suggesting that stenoses of 50 to 69% are prognostically less important. The absence of substantial gradation of infarction risk for lesions >50% may reflect the fact that infarct pathogenesis is more importantly related to the thrombogenic potential of an atherosclerotic lesion than to stenosis severity, once a particular threshold has been crossed. The observation that the group of patients with 90 to 98% stenoses is at particularly high risk for occlusion is supported by the results in a caliper-measured series obtained by Rafflenbeul et al. (14) in which progression to total occlusion occurred within 1 year in all six such patients. Risk of infarction is augmented when multiple stenoses of ≥50% are present.

When assessing the importance of a given coronary stenosis in determining the risk of infarction, one must consider the measurement method in defining percent stenosis. Prior studies (11,12) reported a 5 to 18% variability in visual grading of individual stenoses, dependent in part on the approach used (individual or consensus), the vessel evaluated and the severity of the lesion in question. The results of the present study are in accordance with those of others (11,25) who found that interobserver variability is greatest for lesions of moderate severity and that stenoses are judged to be more severe by the eye than by computer edge-finding algorithms.

Conclusions. Assessment of the maximal percent stenosis for all left anterior descending artery lesions in a given patient predicts risk of anterior infarction in the next 3 years. For patients whose most severe stenosis is <50%, the 3 year risk of infarction is 2%. As the worst stenosis becomes more severe, the risk increases so that for patients with 50 to 89% stenoses the 3 year risk is 6 to 9%. The 3 year risk becomes maximal (>10%) for patients with 90 to 98% stenoses and then declines somewhat (7 to 8%) for patients with a total occlusion without prior infarction. Multiple left anterior descending coronary artery stenoses of >50% severity constitute a particularly severe hazard for subsequent infarction. The extent to which left anterior descending coronary artery revascularization (coronary angioplasty or surgery) is recommended for patients with left anterior descending artery lesions is currently influenced by clinical concerns about the likelihood of anterior infarction and its potential lethal and adverse hemodynamic consequences. The results of this study provide a quantitative angiographic guide to the 3 year risk of anterior infarction in patients who have not undergone coronary revascularization.

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